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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/393,173	09/09/1999	DAVID T. CURIEL	D6163	2338

27851 7590 07/21/2003

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EXAMINER

WEHBE, ANNE MARIE SABRINA

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 07/21/2003

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/393,173

Applicant(s)

CURIEL ET AL.

Examiner

Anne Marie S. Wehbe

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 May 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 5-10 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection on 5/19/03. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/19/03 has been entered. Please note that this response and the accompanying declaration are copies of the after-final amendment received on 2/11/03. The advisory action mailed on 3/19/03, paper no. 16, indicated that this amendment would be entered. Claims 1-3, and 5-10 are pending in the instant application. Regarding claims 1-2, the applicant states on page 5 of the response that claims 1-2 have been canceled. However, there is no record of the applicant ever having requested the cancellation of these claims. The instant response only requests the amendment of claims 3, 7, and 9. As such, claims 1-2 are still considered pending. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in previous office actions.

Claim Rejections - 35 USC § 103

The rejection of claims 1-2 under 35 U.S.C. 103(a) as being unpatentable over WO

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96/25507, published on 8/22/96, hereafter referred to as Seth et al. in view of Sato et al. (Sept. 1, 1998) Mol. Cell. Neurosci., Vol. 12, 65-78 and Anton et al. (1995) J. Virol., Vol. 69, No. 8, 4600-4606, is maintained. The applicant has not presented arguments traversing these grounds of rejection, therefore the rejection of record stands.

Claim Rejections - 35 USC § 112

The rejection of claims 2-3 and 5-10 under 35 U.S.C. 112, first paragraph, is maintained. Applicant's arguments have been fully considered but have not been found persuasive for reasons of record as discussed in detail below. It is noted that applicant's arguments and the declaration by David Curiel were previously addressed in the advisory action mailed to applicants on 3/19/03, see paper no. 16. The response to applicant's arguments and the declaratory data previously provided in the advisory action are reiterated below.

The applicant argues that the data submitted in the declaration by Dr. David Curiel demonstrates the clinical efficacy of the claimed methods *in vivo*. Based on this data and the data present in the specification, in particular examples 6-9, 20-21, and 30-32, the applicant argues that the scope of enablement provided by the specification provides a reasonable correlation to the methods as claimed.

In response, the advisory action stated that in view of the applicant's declaratory data, the scope of enablement was modified to the following scope of enablement: the specification is only

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enabling for methods of treating glioma by intratumoral administration of an inducible recombinant adenovirus encoding a pro-apoptotic bax gene which is placed downstream of a loxP excision cassette and the intratumoral administration of an adenoviral vector encoding cre recombinase followed by the administration of radiation. The applicant's declaratory data, Figure 1, clearly demonstrates that the intratumoral administration of the inducible Ad/bax and Ad/cre alone in the absence of radiation has **no** effect on tumor growth *in vivo*. Therefore, applicant's claims 3-8 clearly lack an essential element necessary for successful treatment of a tumor. Furthermore, the applicant's data is limited to the intratumoral administration of the adenoviral vectors. The specification provides no support for alternative routes of administration. Further, the art at the time of filing as cited in previous office actions, see Verma et al. and French Anderson, teaches the unpredictability in achieving therapeutic levels of gene expression in target cells using various vectors and routes of administration,. Thus, the specification in view of the declaratory data provided does not enable the breadth of the subject matter in applicant's claims.

35 U.S.C. § 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970). The office, having analyzed the specification in direct accordance to the factors outlined in *In re Wands*, namely 1) the nature of the invention, 2) the state of the prior art, 3) the predictability of the art, 4) the amount of direction or guidance present, and 5) the presence or absence of working examples, has presented detailed scientific reasons supported by publications from the prior art (see Verma et al., Crystal et al., and

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Anderson et al.) for the finding of a lack of enablement for scope of the instant methods as claimed. Case law including the Marzocchi decision sanctions both the use of sound scientific reasoning and printed publications to support a holding of non-enablement (see *In re Marzocchi* 169 USPQ 367, and *Ex parte Sudilovsky* 21 USPQ2d 1702). Further, the applicant is reminded that the unpredictability of a particular art area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See *Ex parte Singh*, 17 USPQ2d 1714 (BPAI 1991). Therefore, based on the applicant's own declaratory data that the intratumoral administration of inducible Ad/bax and Ad/cre alone in the absence of radiation has **no** effect on tumor growth *in vivo*, the art recognized unpredictability of gene therapy of disease using currently available vector systems including adenovirus, the lack of sufficient guidance for routes of administration other than intratumoral administration, and the breadth of the claims, it would have required undue experimentation for the skilled artisan to practice the scope of the invention as claimed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37

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CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Monday- Friday from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The technology center fax number is (703) 308-4242, the examiner's direct fax number is (703) 746-7024.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to read 'Anne M. Wehbé', is positioned below the printed name and title.